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| U.S. APPLICATION NUMBER NO. | FIRST NAMED APPLICANT | ATTY. DOCKET NO. |
| 10/519,699 | Thomas N. Horsky | 211843-00032 |
| INTERNATIONAL APPLICATION NO. | | |
| PCT/US03/20197 | | |
| I.A. FILING DATE | PRIORITY DATE | |
| 06/26/2003 | 04/18/2003 | |

27180
 ISIS PHARMACEUTICALS INC
 1896 RUTHERFORD RD.
 CARLSBAD, CA 92008

CONFIRMATION NO. 6928

371 ACCEPTANCE LETTER



OC000000017810368

Date Mailed: 01/11/2006

NOTICE OF ACCEPTANCE OF APPLICATION UNDER 35 U.S.C 371 AND 37 CFR 1.495

The applicant is hereby advised that the United States Patent and Trademark Office in its capacity as a Designated / Elected Office (37 CFR 1.495), has determined that the above identified international application has met the requirements of 35 U.S.C. 371, and is ACCEPTED for national patentability examination in the United States Patent and Trademark Office.

The United States Application Number assigned to the application is shown above and the relevant dates are:

| | |
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| <u>09/14/2005</u> | <u>10/18/2005</u> |
| DATE OF RECEIPT OF 35 U.S.C. 371(c)(1), (c)(2) and (c)(4) REQUIREMENTS | DATE OF COMPLETION OF ALL 35 U.S.C. 371 REQUIREMENTS |

A Filing Receipt (PTO-103X) will be issued for the present application in due course. **THE DATE APPEARING ON THE FILING RECEIPT AS THE " FILING DATE" IS THE DATE ON WHICH THE LAST OF THE 35 U.S.C. 371 (c)(1), (c)(2) and (c)(4) REQUIREMENTS HAS BEEN RECEIVED IN THE OFFICE. THIS DATE IS SHOWN ABOVE.** The filing date of the above identified application is the international filing date of the international application (Article 11(3) and 35 U.S.C. 363). Once the Filing Receipt has been received, send all correspondence to the Group Art Unit designated thereon.

The following items have been received:

- Copy of the International Application filed on 12/23/2004
- Copy of the International Search Report filed on 12/23/2004
- Preliminary Amendments filed on 12/23/2004
- Oath or Declaration filed on 09/14/2005
- Small Entity Statement filed on 12/23/2004
- Copy of references cited in ISR filed on 09/14/2005
- U.S. Basic National Fees filed on 12/23/2004
- Priority Documents filed on 09/14/2005

Applicant is reminded that any communications to the United States Patent and Trademark Office must be mailed to the address given in the heading and include the U.S. application no. shown above (37 CFR 1.5)

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FORM PCT/DO/EO/903 (371 Acceptance Notice)